Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Withdrawn) An antagonist of one or more of Rho family members characterized by the ability to elicit neurite outgrowth from cultured neurons in an assay method, comprising the steps of:

(a) culturing neurons on a growth permissive substrate that incorporates a growth inhibiting amount of Rho family member; and

(b) exposing the cultured neurons of step a) to a candidate Rho family member antagonist agent in an amount and for a period sufficient prospectively to permit growth of the neurons;

thereby identifying as Rho family antagonists the candidates of step b) which elicit neurite outgrowth from the cultured neurons of step a).

2. (Withdrawn) The antagonist according to claim 1, wherein said Rho family members are selected from the group comprising RhoA, RhoB, RhoC, Rac, cdc42 and Rho-associated protein kinase.

3. (Withdrawn) The antagonist according to claim 1, wherein said interaction with the Rho regulatory pathway is via interaction with GTP/GDP cycle.

4. (Withdrawn) The antagonist according to claim 3, wherein the interaction with the GTP/GDP cycle involves GTP/GDP exchange proteins (GEP's); GDP dissociation inhibitors (GDI's); or GTPase activating protein (GAP) to regulate Rho activity.

5. (Withdrawn) The use of antagonists of one or more Rho family members to promote neural growth by inhibiting Rho family members in the central nervous system.

6. (Withdrawn) The use of ADP-ribosyl transferase C3, or other closely related toxins, to promote neural growth by inhibiting one or more Rho family members in the central nervous system.

7. (Withdrawn) The use of a GTPase activating protein that is specific to Rho to convert GTP-bound active Rho to GDP-bound inactive Rho.

8. (Withdrawn) The use of ADP-ribosyl transferase C3 according to claim 5, wherein said related toxins are toxins A or B.

9. (Withdrawn) The use of biologically active fragments of ADP-ribosyl transferase C3, analogs and derivatives thereof, to promote neural growth by inhibiting one or more Rho family members in the central nervous system.

10. (Cancelled)

11. (Withdrawn) The use of genetically mutated forms of Rho, to promote neural growth by inhibiting one or more Rho family members in the central nervous system.

12. (Withdrawn) The use of dominant negative Rho to inactivate Rho, to foster axon growth in the central nervous system.

13. (Withdrawn) The genetically mutated form of Rho according to claim 11, wherein the mutation is in the effector domain, A-37, thereby preventing GTP exchange.

14. (Withdrawn) The use of GDP dissociation inhibitors, or stimulation thereof, to inhibit the dissociation of GDP from Rho and thereby prevent the binding of GTP necessary for the activation of Rho.

15. (Withdrawn) A method for producing Rho antagonists from Rho family members, fragments, analogs of derivatives by peptide synthesis or by recombinant DNA expression of either a truncated domain of Rho family members, incorporating one or more L- or D-amino acid substitutions, or of intact Rho family members using standard recombinant procedures and selecting antagonist characterized by the ability to elicit neurite outgrowth from cultured neurons in an assay method, comprising the steps of:

(a) culturing neurons on a growth permissive substrate that incorporates a growth-inhibiting amount of a Rho family member; and

(b) exposing the cultured neurons of step a) to a candidate Rho family member antagonist agent in an amount and for a period sufficient prospectively to permit growth of the neurons; thereby identifying as Rho family antagonists the candidates of step b) which elicit neurite outgrowth from the cultured neurons of step a).

16. (Withdrawn) The antagonist according to claim 1, wherein derivatives of Rho family members, Rho family members fragments and Rho family members analogs can be generated by chemical reaction of the parent substance to incorporate the desired derivitizing group, such as N-terminal, C-terminal and intra-residue modifying groups that have the effect of masking or stabilizing the substance or target amino acids within it.

17. (Withdrawn) An antagonist of one or more of Rho family members, characterized by the following properties: (a) blocks growth inhibition of neurites by myelin or myelin proteins; and (b) interferes with Rho family members-mediated growth inhibition as competitive but non-functional mimics of endogenous Rho family members.

18. (Withdrawn) A composition comprising a therapeutically effective amount of the composition of claim 1 in a suitable pharmacologic carrier.

19. (Withdrawn) An assay method useful to identify Rho family member antagonist agents that suppress inhibition of neuron growth, comprising the steps of:

(a) culturing neurons on a growth permissive substrate that incorporates a growth inhibiting amount of a Rho family member; and

(b) exposing the cultured neurons of step a) to a candidate Rho family member antagonist agent in an amount and for a period sufficient prospectively to permit growth of the neurons; thereby identifying as Rho family antagonists the candidates of step b) which elicit neurite outgrowth from the cultured neurons of step a).

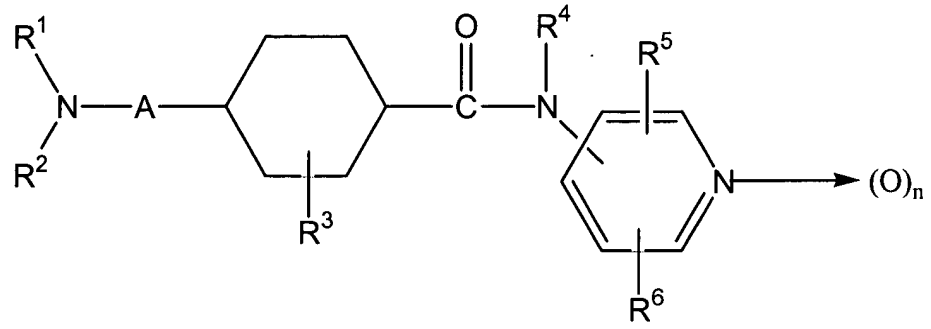
20. (Withdrawn) A kit to test for Rho family antagonists that can be used to promote neurite growth comprising the components necessary to work the method of claim 16, in a suitable container.

21. (Withdrawn) A method to suppress the inhibition of neuron, comprising the steps of delivering, to the nerve growth environment, a Rho family antagonist in an amount effective to reserve myelin inhibition.

22. (Currently amended) A method of promoting neural growth, the method comprising delivery of Y27632[[, or a related compound,]] to a central nervous system tissue.

23. (New) A method of stimulating regenerative growth of damaged neuronal axons in a patient with traumatic nervous system damage, the method comprising delivering directly at a traumatic lesion site in a nerve in a patient, in an amount effective to suppress inhibition of neuronal axon growth, a Rho family antagonist that is:

(i) a compound with the structure



wherein

R^1 and R^2 are the same or different and respectively represent: hydrogen, C_{1-10} alkyl, C_{2-5} alkoxy-carbonyl, amidino, C_{3-7} cycloalkyl, C_{3-7} cycloalkylcarbonyl, or substituted or unsubstituted phenyl, phenylalkyl, bezoyl, naphthoyl, phenylalkoxy carbonyl, pyridylcarbonyl, or piperidyl, the substituent being selected from the group consisting of a halogen, C_{1-4} alkyl, C_{1-4} alkoxy, phenylalkyl, nitro, and amino,

R^1 and R^2 together form unsubstituted or substituted benzylidene, pyrrolidylidene, or piperidylidene, the substituent being selected from the group consisting of a halogen, C_{1-4} alkyl, C_{1-4} alkoxy, phenylalkyl, nitro, and amino,

R^1 or R^2 together with the adjacent nitrogen atom form pyrrolidinyl, piperidino, piperazinyl, morpholino, thiomorpholino, or pthalimido,

R^3 represents hydrogen or C_{1-4} alkyl,

R^4 represents hydrogen or C_{1-4} alkyl,

R^5 represents hydrogen, hydroxy, or C_{1-4} alkyl, or phenyloxy,

R^6 represents hydrogen or C_{1-4} alkyl,

A represents single bond, C_{1-5} straight chain alkylene, or alkylene that is substituted by C_{1-4} alkyl, and

n represents 0 to 1, or

(ii) an optical isomer of the compound or a pharmaceutically acceptable acid addition salt of the compound,

wherein the antagonist stimulates regenerative growth of damaged neuronal axons past the lesion site, and

wherein the antagonist has the ability, when triturated into primary retinal ganglion cells *in vitro*, to produce outgrowth of retinal ganglion cell neurites, the retinal ganglion cells being plated on a growth inhibitory substrate selected from the group consisting of myelin and chondroitin sulfate proteoglycan.

24. (New) The method of claim 23, wherein the antagonist is Y27632.

25. (New) The method of claim 23, wherein the nerve is a nerve in the central nervous system.

26. (New) The method of claim 23, wherein the nerve is a spinal nerve.

27. (New) The method of claim 23, wherein the lesion site comprises a site of surgical injury.

28. (New) The method of claim 23, wherein the regenerative growth comprises a twisted path of growth past the lesion site.

29. (New) The method of claim 23, wherein the regenerative axon growth extends distal to the lesion site.

30. (New) The method of claim 23, wherein the regenerative axon growth is up to 3 millimeter (mm) past the lesion site.

31. (New) The method of claim 23, wherein the nervous system damage is selected from the group consisting of a spinal cord injury, a spinal cord lesion, and a surgical nerve lesion.

32. (New) The method of claim 23, wherein the antagonist is administered with a pharmaceutical carrier or delivery system.

33. (New) The method of claim 32, wherein the carrier is a fibrin adhesive.